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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/510,332	02/22/2000	Charles S. Zuker	2307E-98010US	2643

909 7590 09/11/2002

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EXAMINER

LANDSMAN, ROBERT S

ART UNIT PAPER NUMBER

1647

DATE MAILED: 09/11/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/510,332

Applicant(s)

ZUKER ET AL.

Examiner

Robert Landsman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 94-100 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 94-100 is/are rejected.
- 7) ☒ Claim(s) 94-100 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 13,15.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Sequence Comparison*.

DETAILED ACTION

1. Continued Prosecution Application

The request filed on 9/27/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/510,332 is acceptable and a CPA has been established. An action on the CPA follows.

2. Formal Matters

- A. Preliminary Amendment B, filed 9/27/01, has been entered into the record.
- B. Claims 1-93 have been cancelled. New claims 94-100 have been added. Therefore, claims 94-100 are pending. Claims 94-100 were subject to restriction in Paper No. 20. In Paper No. 23, Applicants elected the hTR4 sequence of SEQ ID NO:7, and its corresponding polynucleotide SEQ ID NO:8, with traverse. Applicants argue that the groups all stem from a common concept and theory and searching all groups (1-72) would not place a serious search burden on the Examiner. This argument has been considered, but is not deemed persuasive. Groups 1-72 are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged. Each group encompasses a SEQ ID NO which encodes a separate and distinct amino acid and encoding nucleic acid molecule. A search for one SEQ ID NO would not necessarily overlap a search for any of the other 71 proteins and encoding nucleic acid molecules. Therefore, claims 94-100 will be examined insofar as they read on SEQ ID NO:7 and 8. This restriction is deemed proper and is, therefore, made FINAL.

MR C. All Statutes under 35 USC not found in this Office Action can be found, cited in full, in a previous Office Action.

3. Specification

- A. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title recites "T2R, a novel family of taste receptors." However, the claims are drawn toward nucleic acid molecules encoding T2R taste receptors. The following title is suggested: Nucleic acid molecules encoding T2R taste receptors.

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4. Claim Objections

A. Claims 94-100 are objected to since Applicants elected SEQ ID NO:7 and 8 in Paper No. 23. However, claims 94, 97 and 98 recite SEQ ID NOs which have not been elected in the present application. It is required that Applicants amend the claims to remove all non-elected SEQ ID NOs. Claims 95, 96, 99 and 100 are objected to since they depend from claims 94, 97 or 98.

5. Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A. Claims 94-100 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are drawn to an invention with no apparent or disclosed patentable utility. Applicants have only demonstrated that the polypeptide encoded for by the claimed nucleic acid is believed to be a taste receptor involved with the detection of bitter tastes (page 4, lines 24-30 of the specification).

However, it is clear from the instant specification that the receptor encoded for by the claimed nucleic acid is what is termed an "orphan receptor" in the art. The instant application does not disclose the biological role of the claimed protein or its significance. The basis that this receptor is a G protein-coupled receptor is not predictive of a use. There is little doubt that, after complete characterization, this receptor protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicants' claimed invention is incomplete.

The instant situation is directly analogous to that of which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

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“The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility,” “[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field,” and “a patent is not a hunting license,” “[i]t is not a reward for the search, but compensation for its successful conclusion.”

The specification and claims disclose 72 distinct polynucleotide and polypeptide sequences of alleged taste receptors. T2R receptors are defined on page 31, lines 10-30 of the specification and characterized in Examples III-IX. In addition, Figures 3-7 of the present invention demonstrate that various T2R proteins do respond to various bitter compounds. However, Applicants have not demonstrated that the protein of SEQ ID NO:7, which is encoded by SEQ ID NO:8, is a taste receptor for bitter compounds, or even a taste receptor at all. Therefore, it appears that Applicants have concluded that the protein of SEQ ID NO:7 is a taste receptor based on its sequence similarity to known taste receptors (page 3, lines 28-30), or to those characterized in Figures 3-7 of the present invention. The assertion that the disclosed proteins have biological activities similar to known taste receptors cannot be accepted in the absence of supporting evidence, because generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene.

Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign

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functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan the utility of the claimed polynucleotides of SEQ ID NO:8, or the encoded polypeptide of SEQ ID NO:7, which are only known to be homologous to taste receptors. Therefore, the instant claims are drawn to a polynucleotide encoding a protein which has a yet undetermined function or biological significance. There is no actual and specific significance which can be attributed to said protein identified in the specification. For this reason, the instant invention is incomplete. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious patentable use for it, or for its encoding nucleic acid. To employ a protein encoded for by a nucleic acid of the instant invention in the identification of substances which bind to and/or mediate activity of said protein (i.e. receptor) is clearly to use it as the object of further research which has been determined by the courts to be a non-patentable utility. Since the instant specification does not disclose a "real-world" use for said protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Furthermore, since the nucleic acids of the invention are not supported by a specific and substantial asserted utility or a well established utility, the vector, host cell and any nucleic acid molecule which hybridizes to SEQ ID NO:8 also lack utility.

6. Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 94-100 are rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

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B. Furthermore, even if Applicants were able to demonstrate utility of the present invention under 35 USC 101, claims 94-100 would still be rejected under 35 USC 112, first paragraph, because the specification, while then being enabling for SEQ ID NO:7 and 8, does not reasonably provide enablement for an isolated nucleic acid encoding a taste receptor wherein said nucleic acid hybridizes to SEQ ID NO:8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of claim 94 is excessive with regard to claiming all nucleic acid molecules encoding taste receptors wherein said nucleic acid molecules “hybridize” under stringent conditions to SEQ ID NO:8, or which hybridize to those nucleic acid molecules encode SEQ ID NO:7. Nucleic acid molecules which “hybridize” to SEQ ID NO:8, or to those encoding SEQ ID NO:7 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides. Similarly, the proteins encoded for by these nucleic acid molecules which hybridize to SEQ ID NO:8, or to those encoding SEQ ID NO:7 would have one or more amino acid substitutions, deletions, insertions and/or additions to SEQ ID NO:7.

Applicants provide no guidance or working examples of nucleic acid molecules which hybridize to SEQ ID NO:8, or of those which hybridize to nucleic acid molecules encoding SEQ ID NO:7, nor do Applicants recite any *functional* limitations of these nucleic acid molecules, or of the proteins which they encode in claim 94, or in any other claim, which would identify the proteins as taste receptors, such as the requirement that the taste receptor must bind to a specific ligand. Furthermore, Applicants do not recite a percent identity limitation, which would limit the scope of the present claims – **without adding new matter**. The recitation of “95%” is preferable. This percent is disclosed on page 31, line 33 of the specification. The recitation in claim 95 of “G protein-coupled receptor activity” is not sufficient to limit the scope of the claim. Furthermore, it is not predictable to one of ordinary skill in the art what functions of these receptors encoded for by the nucleic acids of the present invention would be required to identify these receptors as taste receptors are, other than the recitation that they are generally G protein-coupled taste receptors. Applicants have not provided any disclosure as to what nucleic acids of SEQ ID NO:8 or

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what amino acids of SEQ ID NO:7 would be critical to maintain the structural and functional characteristics of the taste receptor of the present invention.

In summary, even if claims 94-100 did possess utility under 35 USC 101, the breadth of claim 94 is excessive with regard to Applicants claiming all nucleic acid molecules encoding taste receptors wherein said nucleic acid molecules "hybridize" under stringent conditions to SEQ ID NO:8, or which hybridize to those nucleic acid molecules encode SEQ ID NO:7. There is also a lack of guidance and working examples of these nucleic acid molecules. Applicants do not provide a function of these nucleic acid molecules, or a function of the proteins which they encode. These factors, along with the lack of predictability to one of ordinary skill in the art as to what the functions of these nucleic acids, or the proteins which they encode are, other than that they are generally G protein-coupled taste receptors, or what nucleic acids of SEQ ID NO:8, or what amino acids of SEQ ID NO:7 would be critical to maintain the structural and functional characteristics of the taste receptor of the present invention, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed. Claims 95-100 are rejected since they depend from claim 94.

7.Claim Rejections - 35 USC § 112, first paragraph – lack of written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claims 94-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. Nucleic acid molecules which "hybridize" to those polynucleotides encoding SEQ ID NO:8 would have one or more nucleic acid substitutions, deletions, insertions and/or additions to said polynucleotides and would encode for a protein with one or more amino acid substitutions, deletions, insertions and/or additions to the protein of SEQ ID NO:7.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted and the specification and claims do not provide any guidance as to what changes should be

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made. Structural features that could distinguish compounds in the genus from others in the nucleic acid or protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:8, or molecules which hybridize to this polynucleotide, or to those which encode SEQ ID NO:7 (which could be at least thousands of molecules) alone are insufficient to describe the genus.

The specification provides a written description of only SEQ ID NO:7 and 8. No other species are described, or structurally contemplated, within the instant specification. Therefore, one skilled in the art cannot reasonably visualize or predict critical nucleic acid residues which would structurally characterize the genus of nucleic acids encoding the genus of taste receptors claimed, because it is unknown and not described what structurally constitutes any different nucleic acids encoding taste receptors, or nucleic acids encoding taste receptors from any different species, which are further not described. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made; thereby not meeting the written description requirement under 35 USC 112, first paragraph.

8. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 95-100 are rejected under 35 U.S.C. 112, second paragraph, since it fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 95 is confusing since it is not understood what the metes and bounds are of "G-protein receptor coupled activity." For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc.

Furthermore, this claims is confusing since it is not clear if this claim fails to further limit claim 94. Claim 94 recites an isolated nucleic acid encoding a G-protein coupled receptor. Claim 95 depends

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from claim 94 and recites that the nucleic acid of claim 94 encodes a receptor with G-protein coupled receptor activity. Therefore, it is not understood if the nucleic acid of claim 94 encodes inactive G-protein coupled receptors, or if claim 95 fails to further limit claim 94.

B. Claims 95-100 are confusing since they depend from claim 94 and recite "nucleic acid." However, claim 94, from which these claims depend, recite and refer to two different nucleic acids. Therefore, it is not understood to which of these nucleic acids claims 95-100 are referring.

9. Closest Prior Art

A. Adams et al. teach a polynucleotide which is 7.4% identical to SEQ ID NO:8 of the present invention (see the Sequence Comparison which accompanies this Office Action). However, due to the low percentage of overlapping bases, the polynucleotide of Adams et al. would not be expected to hybridize to that of SEQ ID NO:8 of the present invention, especially given the highly stringent hybridization conditions recited in the claims, nor has it been shown to encode a taste G protein-coupled receptor.

10. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
September 09, 2002



SEQ ID NO:8 - Sequence Comparison

AQ308694
 LOCUS AQ308694 742 bp DNA linear GSS 22-DEC-1998
 DEFINITION CITBI-E1-2530B8.TF CITBI-E1 Homo sapiens genomic clone 2530B8,
 DNA
 sequence.
 ACCESSION AQ308694
 VERSION AQ308694.1 GI:4040728
 KEYWORDS GSS.
 SOURCE human.
 ORGANISM Homo sapiens
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
 Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
 REFERENCE 1 (bases 1 to 742)
 AUTHORS Adams,M.D., Rounsley,S.D., Zhao,S., Bass,S., Linher,K., Golden,K.,
 Berry,K., Granger,D., Suh,E., Wible,C., Shizuya,H., Simon,M. and
 Venter,J.C.
 TITLE Use of a random human BAC End Sequence Database for Sequence-
 Ready
 Map Building
 JOURNAL Unpublished (1998)
 COMMENT Contact: Shaying Zhao, William Nierman, Mark Adams
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 Fax: 301 838 0208
 Email: hbe@tigr.org
 Clones are available from Research Genetics (info@resgen.com). BAC
 end search page:
http://www.tigr.org/tdb/humgen/bac_end_search/bac_end_search.html.
 Seq primer: M13-21
 Class: BAC ends.
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 CalTech Human BAC Library D"
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 ORIGIN

Query Match 7.4%; Score 66.4; DB 12; Length 742;
Best Local Similarity 47.8%; Pred. No. 1.9e-05;
Matches 288; Conservative 0; Mismatches 306; Indels 8; Gaps
3;

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Qy 287 tctggtttgtgaccttgctcaatatcttgactgtgtgaagattactaacttccaacact 346
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Db 596 GGACACTCTCTCATCTTAATTTTAGGAAATCCTAAATTGAAACAAAATGCAAAAAGTTC 655

Qy 883 ct 884
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Db 656 CT 657
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